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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,935	02/22/2002	Rebecca A. Cox	4003.001800	4500

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,935	COX ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5/02&11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1/6/04

DETAILED ACTION

1. Applicant's amendment filed on 10/14/03 is acknowledged. Claims 26-32 have been canceled. Claims 1-25 are pending in the application.

Election

2. Applicant's election of Group I claims 1-25 without traverse on 10/14/03 is acknowledged.

Drawings

3 The drawings are objected to for the reasons set forth on the enclosed PTO-948. A proposed drawing correction or corrected drawings are required in reply to this Office action to avoid abandonment of the application.

Information Disclosure Statement

4. Information Disclosure Statements filed on 6/5/02 and 11/24/03 are acknowledged and a signed copy of each is attached to this Office action.

Priority

5. This application claims domestic priority under 35, U.S.C. 119 (e) to provisional application, 60/271,031, (filed 2/22/01.)

Claim Rejections - 35 USC 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-2 and 7-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid segment, composition and a vaccine comprising a first isolated coding region that encodes the

amino acid sequence SEQ.ID.NO: 2 or the nucleic acid sequence SEQ.ID.NO: 1 from *C.immitis* does not reasonably provide enablement for an isolated nucleic acid segment comprising a first isolated coding region that encodes a first peptide of between 18-24 amino acids in length that comprises an amino acid sequence that is at least about 88% or 94% identical to the amino acid sequence SEQ.ID.NO: 2 from any Coccidiodes spp and a composition, vaccine comprising said amino acid sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to an isolated nucleic acid segment or a composition or a vaccine comprising at least a first isolated coding region that encodes a first peptide of between 18 and about 24 amino acids in length that comprises an amino acid sequence that is at least about 88% or 94% identical to the amino acid sequence of SEQ.ID.NO: 2, said nucleic acid encoding the amino acid sequence, SEQ.ID.NO: 2 or nucleic acid sequence, SEQ.ID.NO: 1 said segment is defined as recombinant vector in a recombinant host cell. The recombinant host cell further comprises at least a second isolated coding region that encodes a second, distinct Coccidioides spp. Protein, polypeptide or peptide from SEQ.ID.NO: 4.

The examiner is considering peptides with 88% or 94% as fragments/variants of said sequences.

The instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence

of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is drawn to an isolated recombinant nucleic acid molecule or a composition or a vaccine that encodes the amino acid sequence SEQ ID NO: 2 or nucleic acid sequence SEQ.ID.NO: 1 in a recombinant vector transformed in a host cell expressing peptide or protein. The nucleic acid segment further encodes the full-length protein, SEQ.ID.NO: 4. The specification teaches that immunization with full-length Ag2/PRA recombinant protein (pVR1012-Ag2 1-194) or with truncated Ag2/PRA polypeptide (pVR1012-Ag2 19 -194) and the signal sequence Ag2/PRA 1-18 (pVR1012 Ag21-18) induce protection against challenge infection *C.immitis* (figures 7 and 8) in animals. However, the specification fails to indicate or teach any description of any such signal sequence (Ag2/PRA 1-18) fragments /variants of SEQ.ID.NO: 2 that are able to function as Ag2/PRA 1-18 (pVR1012-Ag2 1-18) against challenge infection or even be able to express a peptide that is suitable for immunizations or bind to antibodies raised against peptide 1-18 and provides no working examples demonstrating (i.e., guidance) enablement for any fragments/variants and uses of the claimed fragments/variants as a vaccine composition.

The state of the prior art indicates that protein chemistry is probably one of the most unpredictable areas of biotechnology and is highly complex. As taught by the prior art (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6), the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis. The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by

glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen ((Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and thus exemplifying the importance of structural components to both biological and immemorial function.

Thus, function or use of fragments/variants must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis. Absent such demonstration, the invention would require undue experimentation to practice as claimed. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed fragments/variants in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the protein renders activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Claim Rejections - 35 USC 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague in reciting "between 18 and about 24 amino acids". Does applicant intend to mean between 18 to 24 amino acids or something else?

Claims 1-2 are vague for the recitation of " at least about 88% " and "at least about 94%" Does applicant intend ~~to mean~~ 88% or 94% or something else?

Claims 10, 11,18 and 22 recite "distinct". It is not clear what applicant means by " distinct" because the specification does not define and the term has many meanings in the Dictionary.

Claim Rejections - 35 USC 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Dugger et al (Biochemical and Biophysical Research Communications 218; 485-489), Accession number: U39835.

The claims are drawn to an isolated nucleic acid segment or a composition or a vaccine comprising at least a first isolated coding region that encodes a first peptide of between 18 and about 24 amino acids in length that comprises an amino acid sequence that is at least about 88% or 94% identical to the amino acid sequence of SEQ.ID.NO: 2, said nucleic acid comprises either encoding the amino acid sequence or nucleic acid sequence, SEQ.ID.NO: 1 said segment is defined as recombinant vector in a recombinant host cell. The recombinant host cell further comprises at least a second isolated coding region that encodes a second, distinct Coccidioides spp. Protein, polypeptide or peptide from SEQ.ID.NO: 4.

Dugger et al disclose an isolated nucleic acid, cDNA (see page 486 under Nucleic acid purification and hybridization and figure 2) comprising a coding region that encodes a peptide that is 100% identical to the amino acid sequence SEQ.ID.NO: 2 (see attached sequence alignment in Accession number: U39835) and nucleic acid sequence is 100% identical to SEQ.ID.NO: 1 (see attached sequence alignment in Accession number: U39835). This isolated nucleic acid segment was constructed in a recombinant vector λ ZAPII and positive plaque was transformed in host cell, E.coli (see abstract and page 485 under Materials and Methods third paragraph through page 486) and the transcript contained an open reading frame encoding a peptide comprising the amino acid sequence MQFSHALIALVAAGLASA and thus read on the claims 1-8. The recombinant host cell further comprises at least a second isolated coding region that encodes a second, distinct Coccidioides spp. Protein, polypeptide or peptide from SEQ.ID.NO: 4 (see internal amino acid sequence, AGVPIDIPPV----AAYL in figure 2). Figure 2 discloses both nucleic acid segment encoding a Coccidioides spp. Protein, polypeptide or peptide and a fusion protein (see last 8 lines). Pharmaceutical carrier would be inherent in the protein mixed with adjuvant. Goats were immunized with a peptide and adjuvant such as complete Freund's and incomplete adjuvant and thus disclosing the composition of the claimed

invention in claims 21-25 (see page 485 under Materials and Methods) including a vaccine. Thus, the prior art anticipated the claimed invention.

12. Claims 1-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhu et al 1996 (Infection and Immunity 64; 2695- 2699), Accession numbers: U32518.

Claims are discussed supra

Zhu et al disclose an isolated nucleic acid, cDNA (see abstract and figure 1) comprising a coding region that encodes a peptide that is 100% identical to the amino acid sequence SEQ.ID.NO: 2 which contains a 18 amino acid N-terminus (see attached sequence alignment in Accession number: U32518) and nucleic acid sequence is 100% identical to SEQ.ID.NO: 1 (see attached sequence alignment in Accession number: U32518). This isolated cDNA nucleic acid segment was ligated into the pGEX-4T-3 in a recombinant vector λ ZAPII and positive plaque was transformed in host cell, E.coli (see abstract and Materials and Methods) and the transcript contained an open reading frame encoding a peptide comprising the amino acid sequence MQFSHALIALVAAGLASA and thus read on claims 1-8. The recombinant host cell further comprises at least a second isolated coding region that encodes a second, distinct Coccidioides spp. Protein, polypeptide or peptide from SEQ.ID.NO: 4 (see internal amino acid sequence, AGVPIDIPPV----AAYL in figure 2). Figure 1 discloses both nucleic acid segment encoding a Coccidioides spp. Protein, polypeptide or peptide and a fusion protein (Table 1). Pharmaceutical carrier would be inherent in the protein mixed with adjuvant. Goats were immunized with a peptide and adjuvant such as complete Freund's and incomplete adjuvant and thus disclosing the composition of the claimed invention in claims 21-25 (see page 485 under Materials and Methods) including a vaccine. Thus, the prior art anticipated the claimed invention.

13. Claims 1-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Jiang et al (Infection and Immunity 1999, 67; 5848-5853),

Claims are discussed supra

Jiang et al disclose an isolated nucleic acid, vaccine and composition comprising nucleic acid encoding a peptide including the nucleic acid sequence, SEQ.ID.NO: 1and amino acid sequence SEQ.ID.NO: 2 and 4 in cDNA pVR1012- Ag2 and IL-12 cDNA, i.e., adjuvant (page 5849, Materials and Methods, figure 1-2 and table2). Thus the prior art discloses a vaccine including the adjuvant. Please note that expression vector pVR1012-Ag2 comprises the SEQ.ID.NO: 1, 2 and 4 as disclosed by Zhu et al 1996 in paragraph # 12 and nucleotide sequence as well as amino acid sequence identical to that of Ag2cDNA as disclosed by Dugger et al 1996 in paragraph # 11. Thus the prior art anticipated the claimed invention.

Status of Claims

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D

1/6/04

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